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Original Article

Management Outcomes of Biliary Complications after Major Liver Resection in a Single Hepato-Biliary Center

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ABSTRACT

Objectives: To determine frequency of various biliary tree complications after hepatectomy, management measures adopted for their management and their outcomes.
Study Design: Prospective longitudinal study.
Place and Duration of Study: Army Liver Transplant Unit, Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan, from Jun 2023 to Jan 2024.
Methodology: A total of 78 patients who underwent major liver resection were included in the study. Patients were assessed for occurrence of biliary complications, management measures adopted for their management and their outcomes.
Results: In this study, 8(10.26%) patients developed biliary complications [5(62.50%) bile leakage, 2(25.00%) anastomosis stricture and 1(12.50%) biloma formation]. 4(80.00%) patients with bile leakage (n=5) were managed by ERCP and 1(20.00%) by PTC. Both patients with anastomosis stricture were managed by ERCP. Patient with biloma was managed by ultrasound guided drainage. All patients were successfully treated 8(100%). Overall 2(2.56%) patients developed biliary peritonitis and both had hepatectomy related bile leakage. Mean hospitalization length was 7.92±1.10 days. Overall mortality rate was 7(8.97%). Among patients who developed biliary complications (n=8); 2(25.00%) died while among patients who did not develop biliary complications (n=70); 5(6.41%) patients died, (p=0.094).
Conclusion: Frequency of biliary complications in patients who undergo major liver resection is 10.26% with biliary leakage being most common biliary complication.

Keywords: Biliary tree, Complications, Hepatectomy, Outcomes.

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INTRODUCTION

Liver is a vital organ of the body that primarily functions as a detoxification center of the body that have the robust ability to regenerate itself.[1] This organ is prone not only to develop primary malignancy (in the form of hepatocellular carcinoma) but also serve as a frequent site of metastatic deposition of tumors located at other sites.[2] In certain cases, where oncologist find the liver tumor to be at stage where its surgical removal may provide beneficial long term outcomes, "hepatectomy" or major liver resection becomes the cornerstone of treatment of both primary malignancy and secondary metastasis of the liver.[3]

"Hepatectomy" is a complex procedure for which a comprehensive knowledge of the functional anatomy of the liver is essential and can be performed through open procedure or by minimally invasive/laparoscopic procedure which has recently been gaining more and more attention.[4] Whatever the technique been used, it is essential that operating surgeons not only should have intricate knowledge, backed by radiological assessment, of the nature of hepatic lesion, its location on the liver and quality of remnant functional liver tissue post-resection.[5] When it comes to the major indication of "hepatectomy", hepatocellular carcinoma is one such indication that constitutes 90% of the primary tumors of the liver with an estimated five-year survival rate approximated up to 15%.[6] Hepatectomy/major liver resection has been found to provide major benefits in liver malignancies, particularly in terms of mortality that has been reported to occur only in 4% of the patients[7] but like any other surgery, "hepatectomy" is associated with a wide variety of complications. Some of these complications include complete and acute failure of liver after resection, intra-abdominal abscess formation and intra-abdominal bleeding. 8 Another important set of complications of "hepatectomy" are

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the ones related to biliary tree with the reported incidence of 11.17%.[8]

Major liver resection/hepatectomy is not a commonly performed surgery in resource depleted country like Pakistan and thus information regarding the surgical complications and outcomes is grossly lacking. A special focus has to be put on biliary complication because whenever there is a damage to the biliary tree, there is a high possibility of leakage of bile into the peritoneal cavity which may lead to "biliary peritonitis" that have been associated with a very high mortality rate reaching as high as 40%.[9] Therefore, this study was conducted with the aim of determining frequency of various biliary tree complications after hepatectomy, management measures adopted for their management and their outcomes.

METHODOLOGY

This Prospective longitudinal study was conducted at "Army Liver Transplant Unit, PEMH, Rawalpindi from June 2023 to January 2024" after obtaining ethical committee approval (ERB #: A/28/ERC/630/23). Appropriate sample size was calculated using "WHO sample size calculator for single population proportions with specified absolute precision".

For calculations, following assumptions were used; "confidence level of significance of 95%", "absolute precision of 7%" and "anticipated frequency of biliary complications after hepatectomy" of 11.17%.[8] This gave a sample size of 78.

$$n = \frac{z^2_{1-\alpha/2} P(1-P)}{d^2}$$

Inclusion Criteria: All patients who were aged 18 years or above, both male and female gender, who underwent major liver resection (≥ 3 segments of liver) or "hepatectomy" were included in this study.

Exclusion Criteria: Patients who were unfit to undergo surgery, who did consent to be part of this study, Child-Pugh class C, ASA IV and those who expired on the operating table were excluded from the study.

Biodata of all the patients was obtained by interviewing the patients who were operated at "Army liver transplant center, PEMH, Rawalpindi". All the hepatectomy procedures were performed by the same team of expert hepatobiliary surgeons with minimum 5 years of experience. Baseline parameters including age, gender, BMI, indication of surgery, Child-Pugh class, ASA status and preoperative radiological status of liver were documented. Operative parameters including operative approach (open or laparoscopic), type of "hepatectomy", operative time and amount of blood loss was documented. After this, presence of any biliary complication that occurred during the surgery was documented. In all these patients, management options used for treating the said biliary complication and their outcomes in terms of successful treatment, biliary peritonitis, hospitalization length and 30-days mortality were documented.

"Data analysis was performed using Statistical package for Social Sciences version 20. Quantitative data (age, BMI, hospitalization length, operative time and amount of blood loss) were represented using Mean±SD. Qualitative data (gender, preoperative radiological status of liver, operative approach, type of hepatectomy, biliary complication, management options used and outcomes) were represented by using percentage and frequency. Hospitalization length between patients who developed biliary complications and those who did not was compared using independent samples t-test. Mortality rate between patients who developed biliary complications and those who did not was compared using Chi-square test. The *p*-value of ≤0.05 was considered as statistically significant".

RESULTS

78 patients were included in this study. Mean age was 45.56±5.03 years. There were 50(64.10%) males and 28(35.90%) were females. Mean BMI was 21.54±3.83 kg/m^2. Most common indication of hepatectomy was "hepatocellular carcinoma (HCC)" 61(78.20%) followed by benign liver mass 11(14.10%) and metastatic disease of liver 6(7.70%). 52(66.67%) had "Child-Pugh class B" and 26(33.33%) had "Child-Pugh class A". 15(19.23%) had ASA status I, 40(51.28%) had ASA status II and 23(29.49%) had ASA status III. Pre-operatively, through radiological status assessment, it was found that 57(73.08%) had cirrhotic liver, 9(11.54%) had normal liver echotexture, 8(10.26%) had fatty liver and 4(5.13%) had congested texture of liver. In terms of operative parameters, 34(43.59%) underwent open hepatectomy and 44(56.41%) patients had laparoscopic hepatectomy. Mean operative time was 255.31±11.32 minutes. Mean intraoperative blood loss was 1034.32±468.77 ml. 7(8.97%) patients had "segmental hepatectomy", 15(19.23%) had "left lateral hepatectomy", 17(21.79%) had "right hepatectomy", 22(28.22%) had "left

extended hepatectomy" and 17(21.79%) had "right extended hepatectomy". Summary of these pre- and intra-operative characteristics is shown in Table-I.

Table-I: Pre- and Intra-Operative Characteristics of Patients (n=78)

Variables	Values
Age	
Mean ± Standard deviation (SD)	45.56±5.03 years
Gender	**n(%)**
Male	50(64.10%)
Female	28(35.90%)
Body mass index (BMI)	
Mean ± Standard deviation (SD)	21.54±3.83 kg/m2
Indication of Hepatectomy	**n(%)**
Benign Liver Mass	11(14.10%)
Hepatocellular Carcinoma	61(78.20%)
Liver metastasis	6(7.70%)
Child-Pugh Class	**n(%)**
A	26(33.33%)
B	52(66.67%)
American Society of Anesthesiologists Status	**n(%)**
I	15(19.23%)
II	40(51.28%)
III	23(29.49%)
Preoperative Radiological Status of Liver	**n(%)**
Normal echotexture	9(11.54%)
Fatty	8(10.26%)
Cirrhotic	57(73.08%)
Congested	4(5.13%)
Approach of Hepatectomy	**n(%)**
Open	34(43.59%)
Laparoscopic	44(56.41%)
Operative Time	
Mean ± Standard deviation (SD)	255.31±11.32 minutes
Intra-operative Blood Loss	
Mean ± Standard deviation (SD)	1034.32±468.77 ml
Type of Hepatectomy	**n(%)**
Segmental	7(8.97%)
Left lateral	15(19.23%)
Right	17(21.79%)
Left extended	22(28.22%)
Right extended	17(21.79%)

Overall, 8(10.26%) patients had biliary complications. Amongst these patients (n=8); 5(62.50%) had bile leakage, 2(25.00%) had anastomosis stricture and 1(12.50%) had biloma formation. Amongst patients who had bile leakage (n=5); 4(80.00%) were managed by ERCP while 1(20.00%) had "percutaneous transhepatic cholangiography (PTC)". Both patients with anastomosis stricture were managed by ERCP. Patient with biloma was managed by ultrasound guided drainage. All patients were successfully treated 8(100%). Overall 2(2.56%) patients developed biliary peritonitis and both had hepatectomy related bile leakage. Mean hospitalization length was 7.92±1.10 days. Among patients who developed biliary complications, mean hospitalization length was 8.25±0.88 days while those who did not develop biliary complications, mean hospitalization length was 7.88±1.12 days (p=0.379). Overall mortality rate was 7(8.97%). Among patients who developed biliary complications (n=8); 2(25.00%) died while among patients who did not develop biliary complications (n=70); 5(6.41%) patients died, (p=0.094). This data is represented in Table-II.

Table-II: Frequency of Biliary Complications, their Management and Outcomes (n=78)

Biliary Complication (n=78)			
Yes 8(10.26%)		**No** 70(89.74%)	
Type of Biliary Complications (n=8)			
Bile leakage		5(62.50%)	
Anastomosis stricture		2(25.00%)	
Biloma		1(12.50%)	
Management options used for Biliary Complications			
Bile leakage (n=5)	ERCP 4(80.00%)	PTC 1(20.00%)	
Anastomosis stricture (n= 2)	ERCP 2(100%)	PTC 0(0.00%)	
Biloma (n=1)	Ultrasound guided drainage 1(100%)	Percutaneous drainage 0(0.00%)	
Outcomes (n=78)			
Successful treatment of biliary complications (n=8)		8(100%)	
Biliary peritonitis		2(2.56%)	
Mean hospitalization length		7.92±1.10 days	
Mortality		7(8.97%)	
Comparison of outcomes (n=78)			
Outcome	**Biliary complications (n=8)**	**No biliary complication (n=70)**	***p*-value**
Biliary peritonitis	2(25.00%)	0(0.00%)	<0.001
Mean hospitalization length	8.25±0.88 days	7.88±1.12 days	0.379
Mortality	2(25.00%)	5(6.41%)	0.094

**ERCP: Endoscopic Retrograde Cholangiopancreatography*

DISCUSSION

Hepatic surgeries are highly complicated procedures that require availability of advance operative facilities as well as surgeon expertise to ensure the favorable outcome in terms of post-operative health of patient and remnant liver. Overtime, with the advancement in the surgical field with immersion of intra-op ultrasonography, robotics and techniques like embolization of the "portal vein" have helped in improving safety of this procedure.[10,11] In Pakistan, which is an underdeveloped nation, specialized centers that can cater these intricate surgeries and provide appropriate post-operative care are quite low in number and thus data regarding the outcomes of this particular surgery is lacking which prompted conductance of this study.

In this study, major indication of performing procedure of hepatectomy was "hepatocellular carcinoma (HCC)". This correlates with the fact that on the global scale, particularly in Asia, incidence of "hepatocellular carcinoma (HCC) is continuously on the rise.[12,13] One of the major reason of rising HCC

incidence in Pakistani population is rising prevalence of chronic viral hepatitis secondary to hepatitis C infection.[14] Majority of the patients in this study who had any pathology of the liver that required hepatectomy were male patients which corresponds to higher incidence of liver diseases in men.[15] Most patients upon radiological assessment performed prior to surgery were found to have liver cirrhosis which corresponded with HCC being the most common reason for hepatectomy in current study. Around half of the patients underwent hepatectomy through laparoscopic approach which correlates with the rising trend of surgeons choosing laparoscopy over open technique to perform hepatectomy.[16]

In terms of biliary complications, approximately 10% of the patients who had "hepatectomy" developed some form of biliary complication amongst which most common was "bile leakage" constituting more than half of the patients with biliary complications. This rate of biliary complications was in coherence with what has been reported in Li *et al.*,[8] who reported this frequency to be around 12%. As compared to present study, however, a meta-analysis states that frequency of biliary leakage amongst the cases of liver resection is very low merely ranging from 0.1% to 1% only.[17] Similarly, in another study conducted by Kar *et al.*,[18] this frequency of bile leakage was reported to be much less as compared to current study at 4.9%. Contrarily, one meta-analysis reported this frequency of biliary complications after hepatectomy to be very high with rates exceeding up to as high as 27.2%.[19] Fortunately, in the present study all the patients were managed successfully who developed any of these complications. Despite this, biliary peritonitis was developed in a small proportion of patients but it only developed in patients who had biliary complication. Hospitalization length was longer in patients who developed biliary complications as compared to those who had uneventful hepatectomy. This finding was in coherence with the finding of Spetzler *et al.*,[19] who also found that such complication significantly lengthen stay at hospital. Overall mortality rate was moderately high in present study. Interestingly, not only in Pakistan but even in developed countries like Germany, information regarding liver surgery related mortality is not well documented.[20] In addition, mortality rate reported in present study was comparable with that observed by Filmann *et al.*,[20] who reported it to be around 10%. The mortality rate was significantly high in those who developed biliary complication. This was congruent with the finding of Martin *et al.*,[21] who found that mortality rate was significantly higher in patients who develop post-liver resection biliary complication.

This study provides important information regarding the morbidity pattern of major liver resection with special focus on the complications associated with "biliary tree". Although the centers that are well equipped with necessary infrastructure to carry out such intricate surgery are limited, it is essential to have documentation of the surgical morbidity and mortality. This study plays a role of stepping stone in this regard. Despite this, there were some limitations of the study that included study being retrospective and dependency on availability of previous record and record being only of single institutions. In future, it is thus recommended that a collaborative effort at regional level should be made to obtain data from multiple such centers so that even better understating of hepatectomy related morbidity and mortality can be achieved.

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CONCLUSION

In conclusion, frequency of biliary complications in patients who undergo major liver resection is 10.26% with biliary leakage being most common biliary complication.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MA & NM: Data acquisition, data analysis, critical review, approval of the final version to be published.

MS & MS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MN & SDH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Itoh T, Miyajima A. Liver regeneration by stem/progenitor cells. Hepatology 2014; 59(4): 1617-1626. https://doi.org/10.1002/hep.26753

2. Swaid F, Downs D, Rosemurgy AS. A practical approach to liver metastasis from unknown primary cancer: What surgeons need to know. Cancer Genet 2016; 209(12): 559-566. https://doi.org/10.1016/j.cancergen.2016.08.004
3. Roayaie S, Jibara G, Tabrizian P, Park JW, Yang J, Yan L, et al. The role of hepatic resection in the treatment of hepatocellular cancer. Hepatology 2015; 62(2): 440-451. https://doi.org/10.1002/hep.27745
4. Lv X, Zhang L, Yu X, Yu H. The difficulty grade of laparoscopic hepatectomy for hepatocellular carcinoma correlates with long-term outcomes. Updates Surg 2023; 75: 881–888. https://doi.org/10.1007/s13304-023-01452-4
5. Faria LL, Darce GF, Bordini AL, Herman P, Jeismann VB, de Oliveira IS, et al. Liver surgery: important considerations for pre- and postoperative imaging. Radiographics 2022; 42(3): 722-740. https://doi.org/10.1148/rg.210124
6. Allaire M, Goumard C, Lim C, Le Cleach A, Wagner M, Scatton O. New frontiers in liver resection for hepatocellular carcinoma. JHEP Rep 2020; 2(4): 100134. https://doi.org/10.1016/j.jhepr.2020.100134
7. Diggs LP, Aversa JG, Wiemken TL, Martin SP, Drake JA, Ruff SM, et al. Patient comorbidities drive high mortality rates associated with major liver resections irrespective of hospital volume. Am Surg 2021; 87(7): 1163-1170. https://doi.org/10.1177/0003134820973368
8. Li B, Qin Y, Qiu Z, Ji J, Jiang X. A cohort study of hepatectomy-related complications and prediction model for postoperative liver failure after major liver resection in 1,441 patients without obstructive jaundice. Ann Transl Med 2021; 9(4): 305. https://doi.org/10.21037/atm-20-5472
9. Lee J, Song O, Park HM, Lee SY, Kim CH, Kim HR. Postoperative bile leakage caused by intrahepatic duct injury during right hemicolectomy: A case report. Medicine 2021; 100(46): e27877. https://doi.org/10.1097/MD.0000000000027877
10. Kokudo N, Takemura N, Ito K, Mihara F. The history of liver surgery: Achievements over the past 50 years. Ann Gastroenterol Surg 2020; 4(2): 109-117. https://doi.org/10.1002/ags3.12322
11. Coletta D, Ossola P, Parrino C, Oddi A, D'Annibale M, Perri P, et al. Robotic liver resections: application of difficulty score systems to an initial experience. is a specific robotic difficulty score necessary? J Laparoendosc Adv Surg Tech 2020; 30(11): 1177-1182. https://doi.org/10.1089/lap.2020.0119
12. Liu Y, Liu L. Changes in the epidemiology of hepatocellular carcinoma in Asia. Cancers 2022; 14(18): 4473. https://doi.org/10.3390/cancers14184473
13. Albarrak J, Al-Shamsi H. Current status of management of hepatocellular carcinoma in the gulf region: challenges and recommendations. Cancers 2023; 15(7): 2001. https://doi.org/10.3390/cancers15072001
14. Khan MR, Begum S. Mandatory multidisciplinary management of hepatocellular carcinoma: Need of the hour in a country with high prevalence of hepatitis C virus infection. J Pak Med Assoc 2021; 71(5): 1455-1457. https://doi.org/10.47391/JPMA.705
15. Nevola R, Tortorella G, Rosato V, Rinaldi L, Imbriani S, Perillo P, et al. Gender differences in the pathogenesis and risk factors of hepatocellular carcinoma. Biology 2023; 12(7): 984. https://doi.org/10.3390/biology12070984
16. Xi C, Zhu M, Ji T, Tan Y, Zhuang L, Yuan Z, et al. A novel difficulty scoring system of laparoscopic liver resection for liver tumor. Front Oncol 2022; 12: 1019763. https://doi.org/10.3389/fonc.2022.1019763
17. Kubo N, Shirabe K. Treatment strategy for isolated bile leakage after hepatectomy: Literature review. Ann Gastroenterol Surg 2019; 4(1): 47-55. https://doi.org/10.1002/ags3.12303
18. Kar I, Qayum K, Sofi J. Indications and complications of hepatic resection patients at Sher-I-Kashmir Institute of Medical Sciences: An observational study. Cureus 2021; 13(11): e19713. https://doi.org/10.7759/cureus.19713
19. Spetzler VN, Schepers M, Pinnschmidt HO, Fischer L, Nashan B, Li J. The incidence and severity of post-hepatectomy bile leaks is affected by surgical indications, preoperative chemotherapy, and surgical procedures. Hepatobiliary Surg Nutr 2019; 8(2): 101-110. https://doi.org/10.21037/hbsn.2019.02.06
20. Filmann N, Walter D, Schadde E, Bruns C, Keck T, Lang H, et al. Mortality after liver surgery in Germany. Br J Surg 2019; 106(11): 1523-1529. https://doi.org/10.1002/bjs.11236
21. Martin AN, Narayanan S, Turrentine FE, Bauer TW, Adams RB, Stukenborg GJ, et al. Clinical factors and postoperative impact of bile leak after liver resection. J Gastrointest Surg 2018; 22(4): 661-667. https://doi.org/10.1007/s11605-017-3650-4